Enteric Coated Thyroid as a Cause Of Relapse in Myxedema

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PATIENTS WITH MYXEDEMA frequently have relapses that are hazardous to them and puzzling to clinicians. Usually such relapses result from failure to continue prescribed replacement hormone, but in the cases here reported the cause was impaired absorption of desiccated thyroid due to the use of enteric coated tablets.

REPORTS OF CASES

CASE 1. A 56-year-old woman received 5 millicuries of I^{131} in June, 1960, as treatment for hyperthyroidism. She had typical signs and symptoms of this disease, including a smooth symmetrical goiter, approximately three times the normal size of the gland. The 24-hour thyroidal uptake of I^{131} was 97 per cent, and the protein-bound iodine (PBI) was 12.2 mcg per 100 ml (total serum iodine (TSI) 15.0 mcg per 100 ml). In August, 1960, the patient was judged to be euthyroid. Symptoms had abated, the thyroid gland had returned to normal size, and the PBI was 4.4 mcg per 100 ml (TSI 5.2 mcg/100 ml).

In September, 1960, the patient had cramps in the lower extremities, sleepiness and rapid gain in weight. On examination, she appeared sluggish, the skin was dry and the speech was slow and indistinct. The PBI was 0.3 mcg per 100 ml (TSI 1.7 mcg). A diagnosis of myxedema was made and replacement thyroid treatment was begun. In December, 1960, on taking 150 mg of desiccated thyroid daily, she was asymptomatic and appeared in a euthyroid state.

In February, 1961, she again had increasing fatigue, sleepiness and gain in weight, although she continued to take the same dose of desiccated thyroid. When examined in May, 1961, she again appeared myxedematous and PBI was 1.6 mcg per 100 ml (TSI 3.1 mcg per 100 ml). It was determined that she had obtained enteric coated thyroid tablets in January, 1961, and had started taking them at about that time. Use of these tablets was discontinued and at first triiodothyronine was prescribed, then, later, uncoated tablets of desiccated thyroid. On a daily dose of between 120 and 180 mg of the latter the patient remained euthyroid. Subsequent PBI determinations ranged between 4.4 and 6.0 mcg per 100 ml.

CASE 2. A 47-year-old woman first developed myxedema in 1944, responded to the administration of desiccated thyroid, but had a relapse when she stopped taking the tablets. When seen in 1948, she presented the classical appearance of severe myxedema. Desiccated thyroid was again administered, and on a daily dose of 120 to 180 mg, the signs and symptoms of the disease disappeared.

During a routine examination in June, 1961, she complained of backache, discomfort in the shoulders and elbows, gain in weight and menstrual irregularity. Upon physical examination dryness of the skin, periorbital edema and pronounced delay in the relaxation phase of the deep tendon reflexes were noted. She was believed to be in a hypothyroid state although taking 180 mg of thyroid daily, the maximum dose that she had been able to tolerate in the past. It was learned that she had been taking the prescribed amount but in enteric coated thyroid tablets, but the exact date of this substitution was uncertain. When uncoated tablets of desiccated thyroid were administered instead, she became euthyroid and remained so on a daily dose of 90 mg.

COMMENT

Enteric coatings have been useful in reducing undesirable gastrointestinal symptoms resulting from the ingestion of drugs which cause local irritation of the gastric mucosa.[4] Furthermore, Talkov and coworkers[5] found that the absorption of coated acetylsalicylic acid tablets was comparable with the uncoated although the analgesic effect of the coated preparations was somewhat delayed. However, the solubility of certain enteric coatings has been shown to vary with composition, temperature, the pH of the surrounding medium and age of the tablet.[1] Some coatings have been shown to dissolve in the stomach, while others resist disintegration and the intact pills are passed in the stool.[3,6] The absorp-

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tion of the agent in these instances is obviously unpredictable, and coating of medications which require critical regulation of dosage would appear to be ill advised. Jefferies[2] described an "irregular response" to enteric coated tablets in patients with myxedema, and advised against their use. It is apparent that in the cases described in this report the relapses were due to impaired absorption of coated medication. It was only by chance that the substitution of coated for uncoated tablets became known.

SUMMARY

In two cases of myxedema the patients had relapses that were traced to the substitution of enteric coated thyroid tablets for the uncoated tablets that had been prescribed.

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Addison's Disease Complicated by Diabetes Mellitus

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ADDISON'S DISEASE or primary adrenal cortical insufficiency is a relatively rare condition. The incidence in this country is about ten cases per million of population, with deaths four in a million.[6] Diabetes mellitus occurs in almost one per cent of the population. Apparently diabetes results from a lack of insulin effect, be it too little insulin as reported in dogs with the pancreas removed by von Mering and Minkowski (1889)[6] or too much insulin antagonist as in the diabetes that follows administration of the pituitary growth hormone.[21] Diabetes may be modified profoundly also by certain other hormonal disturbances such as hypophysectomy (Houssay) and adrenalectomy (Long and Lukens).[6] Although insulin may control the blood sugar level and most of the symptoms in diabetic persons, it does not appear to alleviate the vascular and neural complications nor does it correct the underlying metabolic defect. The exact relationship of diabetes and insulin to glucagon and to the alpha and beta cells of the pancreatic islets seems also to need further elucidation.

Only a few cases of Addison's disease complicated by the subsequent onset of diabetes mellitus have been reported in the world's literature. One reviewer found 24 probable instances,[10] another 19,[20] while several others state or imply that only ten or twelve of these cases are sufficiently well documented to be acceptable.[2,13,16] Arnett[1] seems to have been one of the first to report a case of this type (1927). The reverse sequence or diabetes complicated by subsequent Addison's disease has been reported about 60 times,* but less than half of these cases had postmortem confirmation.[14,19] Ogle reported the first of this type in 1866 and only three additional instances were recorded during the ensuing 50 years.[20] The literature on this subject has been reviewed recently by Bevan and co-workers[3] and all published cases analyzed. No further attempt will be made to consider the recorded cases at this time except to mention that several of these might be regarded as not fully established.

REPORT OF A CASE

A 59-year-old white man was admitted to hospital February 4, 1959, with chief complaint of easy fatigability and dyspnea on exertion. The present illness had begun about 13 years before admission, and during that time he had been in hospital nine times with similar complaints. Numerous diagnostic studies were carried out, chiefly for possible "heart trouble," but no specific cardiac diagnosis was established. Numerous electrocardiograms were reportedly within normal limits. There was a gradual loss of 20 to 30 pounds in weight, and fatigability became increasingly severe. No ankle or pedal edema was noticed and little or no pain in the chest, but at times there was pronounced dyspnea on exertion, substantial "pressure" and difficulty in walking more than one or two blocks. Approximately three years before the present admission, the patient was seen during an episode of unexplained shock with very low blood pressure. Cortisone therapy was started at that time and dramatic improvement promptly ensued. After pertinent laboratory studies, a diagnosis of Addison's disease was made and cortisone therapy was continued regularly thereafter. No sign of diabetes was present at that time.

About two years later a diagnosis of mild diabetes mellitus was also made, after laboratory studies. This condition was at first controlled fairly well by

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*See References Nos. 3-5, 7-9, 11, 12, 14, 15, 17-19, 21.